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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/680,516	10/07/2003	Eugene Mechetner	95,1121-E	5026

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EXAMINER	
HOLLERAN, ANNE L	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 09/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/680,516	MECHETNER ET AL.
	Examiner	**Art Unit**
	Anne L. Holleran	1643

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-6 is/are pending in the application.
  4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5)☐ Claim(s) _____ is/are allowed.
6)☒ Claim(s) 1-6 is/are rejected.
7)☐ Claim(s) _____ is/are objected to.
8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.
10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.
  Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
  Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  a)☐ All b)☐ Some * c)☐ None of:
    1.☐ Certified copies of the priority documents have been received.
    2.☐ Certified copies of the priority documents have been received in Application No. _____.
    3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
  * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
  Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
  Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-6 are pending and examined on the merits.

Priority

2. The instant application is a divisional of application 09/397,233 (now US 6,630,327), which a divisional of 08/752,447 (now US 5,994,088), filed Nov. 15, 1996. The instant application is also a continuation-in-part of application 08/482,670 (now US 6,030,796), which does not provide support for claims 1-6. Although, US 6,030,796 discloses a specific monoclonal antibody, UIC2 (ATCC Accession No. HB11027) which is an antibody encompassed by the instant claims, US 6,030,796 fails to teach or contemplate the genus of antibodies encompassed by the instant claims, which are broadly drawn to antibodies that bind P-glycoprotein in a biochemical conformation adopted in the presence of Pgp-mediated transport substrates or ATP depleting agents. Therefore, the filing date of application no. 08/752,447, Nov. 15, 1996, is the filing date used for comparison with the prior art.

Claim Objections

3. Claim 4 is objected to for the recitation "wherein the heterologous P-glycoprotein comprises an amino acid sequence identified as Seq I.D. No. 1." The sequence of SEQ ID NO: 1 is a nucleic acid sequence, not an amino acid sequence.

Claim Rejections - 35 USC § 112

4. Claims 3 and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3 and 5 are indefinite because they refer to specific changes in the amino sequence of Pgp molecules. The phrase "Pgp molecule" comprises Pgp molecules from any species, whereas the specific changes recited in the claims appear to be relevant to only one species of Pgp protein (the human Pgp protein).

5. Claims 1- 6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is that the disclosure of the specification does not support the breadth of the genus of antibodies encompassed by each of the rejected claims.

Claims 1-6 are product-by-process claims, where the product claimed is an immunological reagent. The immunological reagent is produced by introducing a cell expressing a heterologous P-glycoprotein into an animal syngeneic with the species from which the cell was derived, wherein the heterologous P-glycoprotein is in a biochemical conformation adopted in the presence of Pgp-mediated transport substrates or ATP depleting agents; and producing immune cells in the animal expressing said reagent specific for P-glycoprotein in said biochemical conformation. The immunological reagent may be a monoclonal antibody. The heterologous P-glycoprotein may comprise a mutant P-glycoprotein having an ATPase-specific active site in each half of the Pgp molecule comprising an amino acid residue at position 433 and 1076 of the Pgp amino acid sequence that is an amino acid residue other than lysine. The heterologous P-glycoprotein may comprise an amino acid sequence identified as SEQ ID NO: 1. The heterologous P-glycoprotein may comprise a mutant P-glycoprotein wherein each of the ATPase-specific active site lysine residues of the protein are independently substituted with methionine. The reagent may be specific for P-glycoprotein in a biochemical conformation adopted in the presence of an ATP depleting agent.

The specification teaches a monoclonal antibody UIC2 (ATCC Accession No. HB11027), which is a monoclonal antibody that is specific for human Pgp in a biochemical conformation adopted in certain mutant embodiments of Pgp and in the presence of Pgp-mediated transport substrates and ATP depleting agents.

The claims are drawn to products that, in addition to encompassing the monoclonal antibody UIC2 (ATCC Accession No. HB11027), encompass antibodies that bind to a widely varying genus of polypeptide products. Claims 1-3, 5 and 6 do not specify any particular P-glycoprotein. Thus, for these claims the P-glycoprotein may from any species and may encompass fragments or mutants that are not taught by specification. Additionally, claim 4 encompasses a widely varying genus of polypeptide products because the antibody may bind to a P-glycoprotein that "comprises *an* amino acid sequence identified as SEQ ID NO: 1" (emphasis added). The phrase "comprises an amino acid sequence" is interpreted to mean that the P-glycoprotein may have a sequence that has in common with the sequence of SEQ ID NO: 1 as little as a dipeptide. (For claim 4, this part of the rejection may be overcome by changing the phrase "comprises *an* amino acid sequence" to "comprises *the* amino acid sequence".)

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is for purposes of the 'written description' inquiry, "*whatever is now claimed" (*see page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is now claimed." (See Vas-Cath at page 1116.)

For a claim drawn to a genus, the written description requirement may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant, identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A "representative number of species" means that the species, which are adequately described, are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus (see Official Gazette 1241 OG 174, January 30, 2001). In the instant case, the antibody UIC2 is not representative of the genus encompassed by the claims because the claims broadly recite the use of any P-glycoprotein molecule that may be mutated or from any species. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for making or testing it. One cannot describe what one has not conceived. See

Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. 112, is severable from its enablement provision. (See page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6. Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by either Mechetner-1992 (Mechetner, E.B. et al., Proc. Natl. Acad. Sci., USA, 89: 5824-5828, 1992) or Mechetner-1995 (US 5,434,075; issued July 18. 1995).

The claims are drawn to immunological reagents produced by introducing a cell expressing a heterologous P-glycoprotein into an animal syngeneic with the species from which the cell was derived, wherein the heterologous P-glycoprotein is in a biochemical conformation adopted in the presence of Pgp-mediated transport substrates or ATP depleting agents, and producing immune cells in the animal expressing said reagent specific for P-glycoprotein in said biochemical conformation. The specification discloses that monoclonal antibody UIC2 is an antibody that is specific for Pgp in a biochemical conformation adopted in certain mutant embodiments of Pgp and in the presence of Pgp-mediated transport substrates and ATP depleting agents.

Both Mechetner-1992 and Mechetner-1995 teach monoclonal antibody UIC2. Therefore, either Mechetner-1992 or Mechetner-1995 teach antibodies that are the same as that claimed.

Neither Mechetner-1992 nor Mechetner-1995 recognized that monoclonal antibody UIC2 had the specific property of binding to Pgp in a biochemical conformation adopted in certain mutant embodiments of Pgp and in the presence of Pgp-mediated transport substrates and ATP depleting agents. However, the discovery of an inherent property of a product already disclosed in the prior art is not a basis for patentability.

7. Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Hamada (Hamada, H. et al., Proc. Natl. Acad. Sci. USA, 83: 7785-7789, 1986).

Hamada teaches the MRK16 monoclonal antibody, which is an antibody that binds to human P-glycoprotein (see abstract). The MRK16 monoclonal antibody was made by immunizing BALB/c mice with K-562/ADM cells that are resistant to adriamycin (see page 7785, 2nd col – 7786 first column). Therefore, it appears that K-562/ADM cells express human P-glycoprotein in a conformation adopted in the presence of Pgp-mediated transport substrates or ATP depleting agents. Thus, it appears that MRK16 binds to the same antigen that is bound by antibodies encompassed by the claim.

"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted) (Claim was directed to a novolac color developer. The process of making the developer was allowed. The difference between the inventive process and the prior art was the addition of metal oxide and carboxylic acid as separate ingredients instead of adding the more expensive pre-reacted metal carboxylate. The product-by-process claim was rejected because the end product, in both the prior art and the allowed process, ends up containing metal carboxylate. The fact that the metal carboxylate is not directly added, but is instead produced in-situ does not change the end product.) MPEP 2113.

8. Claims 1-6 are rejected under 35 U.S.C. 102(e) as being anticipated by either Cianfriglia (US 5,776,946; issued Jun. 16, 1998; effective filing date Dec. 15, 1994) or Chu (US 5,503,984; issued Apr. 2, 1996; effective filing date Apr. 13, 1993).

Cianfriglia teaches a monoclonal antibody that binds to P-glycoprotein. The monoclonal antibody was made by injecting BALB/c mice with a vinblastine-resistant variant of the human T-lymphoblastoid CEM cell line. Therefore, it appears that Cianfriglia's antibody binds to a P-glycoprotein that is in a conformation adopted in the presence of Pgp-mediated transport substrates or ATP depleting agents. Chu teaches a monoclonal antibody that binds to P-glycoprotein. The monoclonal antibody was made by injecting BALB/c mice with adriamycin-resistant variant of the human A2780 ovarian carcinoma cell line (see column 4, lines 10-48). Therefore, it appears that Chu's antibody binds to a P-glycoprotein that is in a conformation adopted in the presence of a Pgp-mediated transport substrates or ATP depleting agents.

"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted) (Claim was directed to a novolac color developer. The process of making the developer was allowed. The difference between the inventive process and the prior art was the addition of metal oxide and carboxylic acid as separate ingredients instead of adding the more expensive pre-reacted metal carboxylate. The product-by-process claim was rejected because the end product, in both the prior art and the allowed process, ends up containing metal carboxylate. The fact that the metal carboxylate is not directly added, but is instead produced in-situ does not change the end product.) MPEP 2113.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re*

Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1-6 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 5,434,075. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are drawn to monoclonal antibody UIC2 (ATCC Accession No. HB11027), which is an antibody encompassed by the claims.

10. Claims 1-6 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 5,773,280. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are drawn to a monoclonal antibody produced from a subline of the hybridoma that produces the UIC2 (ATCC Accession No. HB11027), which is an antibody encompassed by the claims.

11. Claims 1-6 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14, and 17 of U.S. Patent No. 6,030,796. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are drawn to cDNA sequences encoding and proteins comprising a protein having the

antigen-binding specificity of monoclonal antibody UIC2 (ATCC Accession No. HB11027), which is an antibody encompassed by the claims.

12. Claims 1-6 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,479,639. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are drawn to antibodies and monoclonal antibodies that bind to the same epitope as UIC2 (ATCC Accession No. HB11027), which is an antibody encompassed by the claims.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official

Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner
September 22, 2006

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER